App of Kenneth E. Miller, Atty Dkt No. 5820.641

US Serial No. 10/660,093, filed 9/11/2003 Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

This listing of claims will replace all prior versions, and listings, of claims in the

application:

Listing of Claims:

1. (Currently Amended) A method for alleviating chronic pain in a subject,

the method comprising the steps of:

administering an effective amount of at least one inhibitor of

neurotransmitter synthesis to a subject suffering from chronic pain

at a peripheral nervous system inflammation site, wherein the at

least one inhibitor of neurotransmitter synthesis is selected from

the group consisting of a glutamine synthetase inhibitor, a

glutamate dehydrogenase inhibitor, a pyruvate carboxylase

inhibitor, a glutamine cycle inhibitor, a glial cell tricarboxylic acid

cycle inhibitor, and combinations thereof; and

wherein the administration of the effective amount of at least one

inhibitor of neurotransmitter synthesis results in inhibition in

synthesis of at least one neurotransmitter in the peripheral

nervous system of the subject at the peripheral nervous

system inflammation site, thereby resulting in a reduction

in glutamate stimulation of peripheral sensory nerve fibers,

2 of 22

Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

whereby a reduction in nociceptive responses at the peripheral

nervous system inflammation site is observed without any

resulting acute pain behavior.

2. (Canceled)

3. (Currently Amended) The method of claim [2] $\underline{\mathbf{1}}$, wherein the at least one

inhibitor of neurotransmitter synthesis is selected from the group consisting of

phenyl acetic acid (PAA), phenylacetyl Coenzyme-A, phenylacetyl Co-A ester,

oxamate, methionine-S-sulfoximine (MSO), phosphinothricin (PPT), 4-N-

hydroxy-L-2,4-diaminobutyric acid (NH-DABA), Delta-hydroxylysine,

bromofuroate, Palmitoyl-Coenzyme-A (Palmitoyl-Co-A), orthovanadate, vanadyl

sulphate, vanadyl acetylacetonate, glutarate, 2-oxoglutarate (a-ketoglutarate),

estrogen, estrogen analogues, pyridine-2,6-dicarboxylic acid, fluoroacetate,

fluorocitrate, and combinations and derivatives thereof.

4. (Previously Presented) The method of claim 1, wherein the subject is a

human.

3 of 22

Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

(Previously Presented) The method of claim 1, wherein the step of 5.

administering an effective amount of at least one inhibitor of neurotransmitter

synthesis to a subject suffering from chronic pain at a peripheral nervous

system inflammation site is further defined as locally administering an effective

amount of at least one inhibitor of neurotransmitter synthesis to a subject

suffering from chronic pain at a peripheral nervous system inflammation site.

6. (Previously Presented) The method of claim 1, wherein the step of

administering an effective amount of at least one inhibitor of neurotransmitter

synthesis to a subject suffering from chronic pain at a peripheral nervous

system inflammation site is further defined as injecting an effective amount of

at least one inhibitor of neurotransmitter synthesis to a subject suffering from

chronic pain at a peripheral nervous system inflammation site.

(Currently Amended) The method of claim 1, wherein the step of 7.

administering an effective amount of at least one inhibitor of neurotransmitter

synthesis to a subject suffering from chronic pain at a peripheral nervous

system inflammation site is further defined as topically applying an effective

amount of at least one inhibitor of neurotransmitter synthesis to a subject

suffering from chronic pain at a peripheral nervous system inflammation site.

4 of 22

Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

8. (Currently Amended) The method of claim 1, wherein the step of

administering an effective amount of at least one inhibitor of neurotransmitter

synthesis to a subject suffering from chronic pain at a peripheral nervous

system inflammation site is further defined as orally administering an effective

amount of at least one inhibitor of neurotransmitter synthesis to a subject

suffering from chronic pain at a peripheral nervous system inflammation site.

(Previously Presented) The method of claim 8, wherein the effective 9.

amount of at least one inhibitor of neurotransmitter synthesis is in the form of

a prodrug.

10. (Previously Presented) The method of claim 8, wherein the effective

amount of at least one inhibitor of neurotransmitter synthesis demonstrates

substantially no penetration across the central nervous system blood brain

barrier.

11. (Previously Presented) The method of claim 1, wherein the

administration of the effective amount of at least one inhibitor of

neurotransmitter synthesis results in a reduction in nociceptive responses at the

5 of 22

Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

peripheral nervous system inflammation site for at least two days without any

resulting acute pain behavior.

12-18. (Canceled)

19. (Currently Amended) A method for alleviating acute and chronic pain in

a subject, the method comprising the steps of:

administering an effective amount of at least one inhibitor of

neurotransmitter synthesis to a subject suffering from acute and

chronic pain at a peripheral nervous system inflammation site,

wherein the at least one inhibitor of neurotransmitter synthesis is

selected from the group consisting of a glutamine synthetase

inhibitor, a glutamate dehydrogenase inhibitor, a pyruvate

carboxylase inhibitor, a glutamine cycle inhibitor, a glial cell

tricarboxylic acid cycle inhibitor, and combinations thereof;

administering an effective amount of at least one compound having

analgesic effects to the subject at the peripheral nervous system

inflammation site; and

wherein the administration of the effective amount of at least one

inhibitor of neurotransmitter synthesis results in inhibition of at

6 of 22

<u>least one neurotransmitter in the peripheral nervous system</u>

of the subject at the peripheral nervous system

inflammation site, thereby resulting in a reduction in

glutamate stimulation of peripheral sensory nerve fibers,

and the administration of the effective amount of at least one

compound having analgesic effects results in a decrease in

nociceptive responses at the peripheral nervous system

inflammation site without any resulting acute pain behavior.

20. (Canceled)

21. (Currently Amended) The method of claim [20] 19, wherein the at least

one inhibitor of neurotransmitter synthesis is selected from the group consisting

of phenyl acetic acid (PAA), phenylacetyl Coenzyme-A, phenylacetyl Co-A ester,

oxamate, methionine-S-sulfoximine (MSO), phosphinothricin (PPT), 4-N-

hydroxy-L-2,4-diaminobutyric acid (NH-DABA), Delta-hydroxylysine,

bromofuroate, Palmitoyl-Coenzyme-A (Palmitoyl-Co-A), orthovanadate, vanadyl

sulphate, vanadyl acetylacetonate, glutarate, 2-oxoglutarate (a-ketoglutarate),

estrogen, estrogen analogues, pyridine-2,6-dicarboxylic acid, fluoroacetate,

fluorocitrate, and combinations and derivatives thereof.

7 of 22

App of Kenneth E. Miller, Atty Dkt No. 5820.641

US Serial No. 10/660,093, filed 9/11/2003 Examiner: K. Srivastava; Art Unit: 1657

Response to Office Action dated 6/6/2007

22. (Original) The method of claim 19 wherein, in the step of administering

an effective amount of at least one compound having analgesic effects, the at

least one compound having analgesic effects is a glutamate antagonist or an

inhibitor of glutamate binding to glutamate receptors on peripheral sensory

nerves.

23. (Currently Amended) The method of claim 19, wherein the administration

of the effective amount of at least one inhibitor of neurotransmitter synthesis

and the administration of the effective amount of at least one compound having

analgesic effects results in a decrease in nociceptive responses at the

peripheral nervous system inflammation site that last for a period of at least

two days without any resulting acute pain behavior.

8 of 22